# Ocular and other comorbidities in HIV positive orphans in Myanmar

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#### **Abstract**

**Objectives:** This study is to explore the ocular manifestations, nutritional status and other concurrent comorbidities of the HIV positive orphan in relation to gender.

**Method**: It is a cross sectional study done in one orphanage home in Yangon, Myanamr. 60 children included in the study. Data collection methods are record review, interview and physical, anthropometric and ophthalmic examination. Pretested precoded profoma is used for record review and record of examination findings. WHO BMI and MAC standard are used for assessment of Nutritional status.

**Results:** 28 boys and 32 girls included in this study. Age ranged from 2 years to 15 years. 36 children are HIV stage 1, 16 in stage 2 and 7 in stage 3 and only one in stage 4. Nutritional problem is seen in 60% of the children. Ocular morbidity is seen in only 3children (5.1%). Other systemic comorbidities were seen in 23 children (37.7%). There are no significant differences in CD4 count, HIV status and provision of ART among male and female children.

**Conclusions**: This study showed ocular manifestations in paediatric HIV population is low. Majority of children had nutritional problems. Tuberculosis and otitis media were seen in small proportion.

**Keywords:** HIV, Orphan, Ocular manifestation, ART, TB, Nutritional status

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#### Introduction

In Myanmar, the number of people living with HIV/AIDS (PLWHA) was estimated at 238,000 and 17,000 deaths due to AIDS- related diseases in 2009. Many innocent children became orphans due to AIDS and even worst they were infected through pregnant mother to child transmission. It is estimated that the worldwide number of paediatric HIV raced up to 2.5 million with newly infected cases of 370,000 in the year 2009. In 2008, there were total 39 cases of paediatric HIV reported with 2.8% rate of mother to child transmission in Myanmar.

In early era of epidemic, AIDS- related mortality and morbidity were high but with advent of anti-retroviral therapy it was dramatically reduced notably in past decade. ART had changed the survival and pattern of disease among people living with HIV/AIDS (PLWHA) including children. Care of PLWHA especially children is important to make them independent and leading a productive life in the future.

Although low birth weight is not attributed to HIV infection of the baby born to HIV positive mother, it contributes to growth failure in children. Failure to thrive is seen in 20-70% of infected children.<sup>3</sup> Under nutrition rates among HIV children are increasing and orphans are mostly affected.<sup>4</sup> As malnutrition is a contributing factor to onset of immune deficiency and opportunistic infection, it is important indicator for comorbidity and mortality of HIV infected children.

Keeping in mind of these facts, there are concerns for the orphanage children who are HIV positive. Being marginalized through stigma and discrimination, these vulnerable children face several challenges particularly lack of access to basic care and preventive needs. But there is no study and publication in that area in Myanmar. This study fills the gap by assessing the ocular and other comorbidity together with their nutritional status of HIV positive children.

# **Materials and Methods**

A total of 60 children from Orphanage Home for HIV positive children in Yangon, Myanmar were involved in this study. All of them were born from sero-positive mothers and they were diagnosed by screening test (ELIZA) and confirmed by western blot test. The exact age of sero-positivity was not available as most of them became orphans during early childhood.

All children underwent complete ophthalmic examination which included best corrected visual acuity, adnexal examinations, ocular motility, anterior segment examination, pupillary light reflexes and posterior segment examination using slit lamp, 90D lens and indirect ophthalmoscope. Visual acuity testing was done using Snellen chart. Landolt C Chart was used for younger children between 2 to 5 years.

Data collection method included record review, interview, physical and anthropometric measurements. WHO BMI and MAC standard are used for nutritional assessment. For HIV staging, revised clinical staging and immunological classification of HIV related disease in children WHO 2007 was used.

#### **Results**

# General:

Of 60 HIV positive orphans examined in this study, there were 28 boys and 32 girls. Age ranged from 2 years to 15 years, 26.7% were under five, majority 56.7% were between 6-10 years and 16.6% between 11-15 years of age. There was higher proportion of female (61.4%) in older age group (above 5 years old) compare to that of male (38.6%). Regarding the clinical staging of HIV, 36 children (60%) were in stage 1, 16 (26.7%) in stage 2 and 7 (11.7%) in stage 3 and only one (1.7%) in stage 4.

All children were on regular follow up with the clinical service centres run by both government and non-governmental organizations and were monitored for CD4 counts and systemic manifestations. Antiretroviral therapy (ART) was started whenever necessary. Recent CD4 count is not available in 18 children (30%) as it was kept in health office record for the clinic and not informed to care-givers. Among 42 children whose recent CD4 count available, only 3 children (5%) has low CD4 less than 200 and 39 (65%) has CD4 above 200. Out of 60, 45 children (75%) were currently on ART with duration ranged from 6 months to 3 years. There were no significant differences in CD 4 count and HIV staging among male and female.

# Ophthlmic:

A total 102 eyes of 51 children (85%) showed a best corrected visual acuity of 6/12 and better. 8 eyes had visual acuity ranged from 6/18 to 6/60. One children had one eye blind (no perception of light) and 3/60 in the other eye.

Only 3 children (5.1%) have ocular manifestations. Case one presented with ocular adnexal involvement with extensive molluscum contagiosum infection. Case two had old geographical corneal scar in left eye. Case three had bilateral involvement. Right eye showed old tractional retinal detachment involving the macular area and left eye had perivascular sheathing.

#### Others:

Nutritional problem is seen in 60% of the children. Although overweight and obesity is not common among HIV positive children, (10%) of children in this study were in this category and 50% were either under nutrition or malnutrition; specifically 23.3% had malnutrition and 26.7% had under weight, while 8.3% found to be overweight and 1.7% found to be obesity. It

was found that 45% of children were stunted and 18.3% were short stature. No significant difference in nutritional status nor proportion of short stature and stunted was seen among boys and girls. There is no association of HIV staging and nutritional status.

Systemic comorbidities were seen in 24 children (40%), 16 (26.6%) had chronic otitis media and 8 (13.3%) had pulmonary tuberculosis receiving antituberculous therapy. Out of 8 children with TB, 5 of them were taking ART at the time of examination. There were three children who were not on ART, two had recent CD4 results which were 229 and 433; the other one did not have recent CD4 count, was 2 years old and found to be underweight. It was said he was on regular check up and due to his CD 4 count and general condition doctor decided not to start ART. Among 5 children receiving ART with HIV-TB coinfection, two were malnourished and one was underweight. A boy who was 8 years old with stage 4 disease was found to be malnourished and his CD4 count was 16. He had nephropathy and had ocular involvement in both eye (Case Three). The rest of HIV- TB coinfection children had CD4 count higher than 200. Since there were only 8 TB patients, statistical application cannot be made to explore the association with socio demographic characteristics.

# **Discussion**

Among the study children, there is higher proportion of female (61.4%) in older age group (above 5 years old) compare to that of male (38.6%). Although acceptance criteria for male and female were the same, why female patient reach to orphanage at older age compare to male is quite interesting. Is it due to delay diagnosis? Or is it due to more protection by society for female? These are the things to explore.

Paediatric cases of AIDS were first reported in 1982.<sup>5</sup> Since then there were growing number of cases worldwide. Paediatric HIV differs from that of adult in various ways including mode of transmission of infection, incubation period and clinical course.<sup>6</sup> 19% of paediatric HIV cases acquired infection through transfusion of blood and blood products whereas 78% were infected perinatally.<sup>6</sup> It was evident that virus can be transmitted via transplacental route<sup>7,8</sup> as well as postnatally through breast milk.<sup>9,10</sup> With specific ART, risk of mother-to-child transmission (MTCT) is approximately 5% in breastfeeding mothers and is less than 2% in non-breastfeeding populations. However the risk of MTCT is increased to 20% to 45% without intervention.<sup>11</sup> In this study, all 60 children were infected from pregnant mother to child transmission. That shows the needs for strengthening of antenatal HIV screening and prevention of mother to child transmission (PMCT) activities.

Majority of children (60%) were still asymptomatic. The average age of onset of symptoms in perinatally infected infants is 9 months although few children can be asymptomatic for years. In children the incubation period has increased with each surveillance year which may

even longer than 7 years.<sup>12</sup> The orphans included in this study, although infected perinatally from seropositive pregnant mother only 40% is symptomatic. Detail study on incubation period for AIDS in children infected with HIV perinatally will give supportive information for evaluation of ART therapy.

This study revealed that ocular involvement is 5.1%. Summary of three patients with ocular involvements is shown in Table 1. Various study reported that incidence of ocular manifestations in paediatric HIV between 20- 54% <sup>6, 13, 14,15</sup> It is postulated that two mortality peaks associated with perinatally infected children, one at the age of seven months and another between two and three years. <sup>16</sup> Generally, older children who survived beyond three years had better prognosis. <sup>16</sup> All children in our study were older than 3 years except two children who were between 2-3 years at the time of examination. Some of the ocular manifestations are temporary in nature therefore the proportion of ocular manifestations in those who survived from the two mortality peak may lower than that of children at the peak. That is the reason the proportion of the children with ocular manifestation is lower than other study. Another possibility is examination was done once and statistics may higher if there is follow up examinations.

The first patient presented with ocular adnexal involvement. She is 6 years old girl with stage 2 disease. She has extensive infection with molluscum contagiosum involving eyelids and face. (Figure 1) Her CD4 count is 78, currently on ART. Molluscum contagiosum is a highly contagious dermatitis caused by a poxvirus. Both the skin and the mucous membranes may be affected with painless small and multiple umbilicated lesions. In HIV positive persons, molluscum contagiosum are more common and tends to be more extensive with larger, more numerous, and more rapidly growing lesions. Eyelid involvement is seen in up to 5 % of HIV positive patients. There were studies reported that molluscum contagiosum lesions of the eyelid presented as the initial manifestation of HIV.

Case two is 11 years old boy who has healed geographical corneal scar in left eye, CD4 count is 1303 with stage 2 disease, not on ART at the time of examination. Corneal infections occur in less than 5 percent of HIV-infected patients<sup>21</sup>. Varicella–zoster virus and herpes simplex virus are the most common causes of infectious keratitis.<sup>22</sup> Keratitis related to varicella–zoster virus infection is often characterized by the presence of herpes zoster ophthalmicus, although the dermatitis may be mild or even absent.<sup>23,24</sup> Herpes simplex keratitis is usually associated with corneal scarring.<sup>22</sup>

Case three is 8 years old boy. Relative afferent pupillary defect was detected in his right eye. Dilated fundus examination revealed pale optic disc and old tractional retinal detachment involving macular area in right eye resulting in blindness in that eye (Figure 2A) which was undiagnosed. The fellow eye had feature of perivascular sheathing in the fundus (Figure 2B). There were no signs of active inflammation detected in both eyes. He was in stage 4 disease with low CD4 of 16, being treated with ART for more than a year. He had systemic comorbidities such as nephropathy and tuberculosis receiving antituberculous treatment currently.

The exact cause of tractional retinal detachment remains uncertain but perivasculitis may be possible explanation. Another possibility is periphlebitis of the retinal blood vessels related to systemic tuberculosis. One study reported that perivasculitis of peripheral retinal vessels is the most common finding in paeditric African population, observed in 38% of patients. None of 60 HIV seropositive children in this study showed cotton wool spots and CMV retinitis, the most common ocular manifestations in adults and it correlates with other studies done in paediatric HIV groups. 13,14

Regarding the nutritional status, like in other countries<sup>3,25,26</sup> proportion of mal nutrition were high (23.3%) in this study. This study conducted the anthropometric measurement for once and cannot observe the trend of changes in weight and height. Regular growth and development monitoring of children especially those (26.7%) who were detected as underweight from this study, is necessary to detect progress of the treatment as well as nutritional status.

Although overweight and obesity is not common among HIV positive children, one study pointed out that fat deposition can occur as side effect of HAART.<sup>27,28</sup> Therefore those children who were overweight (8.3%) and one child who was obese (1.7%), should not be neglected. This study did not detect lipid profile and measure lean body mass, however if financial situation and available facilities are favourable these test are worth trying to detect the side effect of HAART.

Regarding height for age, the proportion of short stature (18.3%) and stunted (45%) were similar to Nigerian study<sup>25</sup> but lower than that of Malawi orphan<sup>26</sup> and higher than that of orphan in china<sup>29</sup>. Short stature may link to genetic condition and it is difficult point out the influence of HIV on growth or genetic factor. Many studies showed that HIV positive orphans are more vulnerable to develop malnutrition and growth failure and emotional support from care givers is necessary to reduce it.<sup>25,26,29</sup>

Other systemic comorbidities observed in our study were otitis media and pulmonary tuberculosis. In HIV infected children, Severe recurrent infections such as otitis media, sinusitis, and pneumonia caused by routine bacteria such as *Haemophilus influenza* and *Streptococcus pnemoniae* have been reported as a characteristic of paediatric HIV disease<sup>30</sup> and are common, more persistent and refractory to treatment. Since this is the cross sectional study, the examination of the children was done once therefore acute infection might not be present at the time of study.

A total of 16 children (26.7%) had chronic recurrent otitis media but aetiological agents were not identified due to lack of laboratory resources as well as restraint of funding. This proportion was higher than the study done in India where 8.1% of children attending an HIV clinic in Chennai had ear infection.<sup>32</sup>

Pulmonary tuberculosis co-infection was present in 8 children (13.3%) Details of HIV-TB coinfection cases are summarized in Table 2. The proportion in this study was lower than

that of Nigerian study<sup>33</sup> and that of the studies done in India<sup>32,34</sup> where the proportion were 19.5 %, 55% and 67% respectively. Despite half of the children in this study were either underweight or mal nourished, majority of children were still free of TB. Myanmar is one of the countries having rates of HIV higher than 1% in general population and the highest HIV/TB coinfection rates in South East Asia region.<sup>35</sup> It is well known that tuberculosis is serious threat to PLWHA. Children also have an increased risk of developing primary progressive TB because of the associated severe immune suppression resulting from their young age and HIV. Extrapulmonary TB is seen more often in HIV-infected children.<sup>36</sup> Tuberculosis can be the first manifestation of AIDS and one of the leading causes of death<sup>37</sup>. Thus early detection and appropriate treatment is important. Continuous monitoring of weight is the best option for early detection of tuberculosis as severe weight loss can be the only clinical feature of co infection of TB in HIV positivie children<sup>37</sup>.

Nephropathy is seen in a child (case three with eye involvement) with stage 4 disease with CD4 count 16 who had pulmonary tuberculosis and ocular involvement as well. In approximately 15% and 5% of HIV-infected children with AIDS and those without AIDS, respectively, the disease progresses to HIV nephropathy. HIV nephropathy is more common in African American children than in others.<sup>38</sup>

There were no significant difference in HIV status, nutritional status, and access to ART of boys and girl in this orphanage. That is a good sign for gender equality.

# **Limitations of the Study**

There were limitations to this study. First, we could not obtain the data regarding the treatment with ART in infancy which influence the clinical outcome. Second, previous CD 4 count before ART treatment was not available so that effect of treatment on CD 4 count cannot be analysed. Third, but not the least, this study is done in orphanage home so that it reflects the picture of institutional life of HIV positive orphanage children and finding may or may not be generalized to all HIV positive children.

# **Conclusion**

In this orphanage, HIV positive children were well taken care and arranged for ART treatment. There is no gender difference in availability of services as well as morbidity of children. However, being a cross sectional study, serial monitoring of nutritional status and ocular examination of the children cannot be done, thus cannot get the complete picture of nutritional situation of the children. It is recommended that future study of this kind should do serial physical examination, records review for information about past infection as well as trend

of growth and development. Findings from this study pointed out importance of regular monitoring of growth and nutritional status as well as regular ocular examination of the children. It also pointed out to pay attention on over nutrition as well as under nutrition.

Conflict of Interest: None declared.

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Table 1: Ocular lesions in HIV- serpositive orphans

Sex/Age (years)	Stage	Ocular Findings	CD4 Counts	ART
F/6	2	Extensive molluscun infection over face and eyelids	78	(+)
M/11	2	Left geographical corneal scar	1303	(-)
M/8	4	Right eye - blind, pale optic disc Tractional membrane over macular area Left eye - perivascular sheathing	16	(+)

Table 2: Clinical summary of HIV/TB co-infection cases

Sex/Age (years)	Stage	CD4 count	ART	Nutritional status
M/2	3	NA*	(-)	Underweight
F/2	3	433	(-)	Underweight
M4	3	685	(+)	Normal
F/6	3	290	(+)	Malnutrition
F/6	3	301	(+)	Underweight
M/8	4	16	(+)	Malnutrition
F/10	3	229	(-)	Normal
F/15	3	203	(+)	Underweight

NA - Not Available



Figure 1. A girl with extensive molluscum contagiosum lesion



Figure 2. Fundus appearance of ocular case three: A. Right eye B. Left eye